REMARKS/ARGUMENTS

Claim 24 has been cancelled. No new matter has been added by way of amendment. Reexamination and reconsideration of the claims are respectfully requested.

The Rejection of Claims Under 35 U.S.C.§112, First Paragraph, Should Be Withdrawn

The Office Action (9/24/03, page 2, #2) has again rejected claims 1 and 9-23 under 35 U.S.C. §112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention."

Applicants note that claim 24 has been cancelled and that consequently all of the claims are limited to SEQ ID NO:1. Applicants respectfully disagree with the conclusion in the Office Action that the remaining claims do not meet the written description requirement.

Applicants respectfully submit that the Examiner is applying an extraordinarily high standard of written description to the present claims, a standard that is not properly based on case law or on the statute. First, Applicants note that the *Guidelines for the Examination of Patent Applications Under the 35 U.S.C. § 112, ¶ 1, "Written Description" Requirement* state that "[d]escription of an actual reduction to practice of a biological material may by shown by specifically describing a deposit made in accordance with the requirements of 37 CFR 1.801 *et seq.* (66 Fed. Reg. 1099, 1106 (2001)). Further, under *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 63 U.S.P.Q.2d 1609 (Fed. Cir. 2002), the written description requirement is met by reference in the specification to a deposit in a public depository. Here, Applicant makes reference in the specification to the plasmid containing the genomic DNA insert corresponding to SEQ ID NO:1 (ATCC 97791; see specification page 38).

Further, a description can be by structure, formula, chemical name, or physical properties. *See Ex parte Maizel*, 27 USPQ2d 1662, 1669 (B.P.A.I. 1992), *citing Amgen v. Chugai*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). Here, the sequence listing sets forth the actual structure of SEQ ID NO: 1. Applicants have thus provided a structural definition of the sequences of the invention by providing the nucleotide sequence set forth in SEQ ID NO:1.

Because claims 1 and 9-23 are drawn to this sequence, the subject matter of claims 1 and 9-23 satisfies the written description requirement and the rejection of these claims should be withdrawn.

The Office Action (page 3) "[maintains] that Applicant has not described a promoter" because "enhancer and inhibitor elements can occur at great distances from the transcription start site." Applicants claim 1, which was amended to clarify the scope of the claim, only requires that the promoter sequence drives expression of a gene in a plant cell. Thus, the claimed subject matter does not encompass every regulatory element which might affect gene expression. Rather, the claims are drawn to a promoter sequence that drives expression of a gene in a plant cell wherein said promoter sequence comprises the sequence set forth in SEQ ID NO:1.

One of skill in the art would agree with the assertion that the claimed sequence is a promoter sequence that drives expression of a gene in a plant cell. As noted in the Office Action (page 3), the sequence of SEQ ID NO:1 corresponds to the upstream region of the *lls1* gene, and it is known in the art that such regions have promoter activity. See, *e.g.*, Desh Pal Verma reference previously submitted. Despite this knowledge in the art, the Office Action (page 3) makes a number of unsupported statements to support the conclusion that "Applicant has not described a promoter." Because these statements are not supported by any evidence of record, a *prima facie* case of lack of enablement has not been established. If the rejection of claims 1 and 9-23 is maintained on this ground, Applicants respectfully invite the Examiner to support this statement by submitting an affidavit under 37 C.F.R. § 1.104(d)(2).

In view of the structural definition provided and the biological deposit of the claimed subject matter described above, Applicants respectfully submit that they have described the claimed promoter sequence and that this rejection of the claims for lack of written description should be withdrawn.

The Office Action (9/24/03, page 4, #3) reiterates the rejection of claims 1-23 and rejects new claim 24 as "containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." Applicants note that claim 24 has been canceled.

However, in maintaining these grounds for rejection, the Office Action disregards not only Applicants' arguments but also the case law and guidelines cited in those arguments. Applicants respectfully traverse this rejection and submit that the Office Action is applying an extraordinarily high standard of enablement to the present claims, a standard that is not properly based on case law or on the statute.

In the previous Response, Applicants discussed that the claims are enabled by the disclosure. Applicants discussed (Response of January 11, 2001, particularly pages 6-8) that those of skill in the art, provided the guidance in the present specification, could readily make and use the invention. Applicants noted (Response of January 11, 2001, particularly pages 7-8) that the knowledge in the art supports the conclusion that the sequence of SEQ ID NO:1 has promoter activity. In the instant specification, Applicant has provided assays and procedures by which those of skill in the art may readily determine whether the claimed sequence has promoter function (see particularly the Examples at pp. 25-42). Such assays are also known in the art, so that one of skill in the art can readily determine whether a sequence is capable of driving transcription in a plant cell.

Disregarding this support, the Office Action states that "[t]he specification has provided no evidence of promoter activity for the disclosed nucleotide sequence" and states that "it is critical that empirical evidence be provided by Applicant of promoter activity by the disclosed upstream region." However, it is established in the art that a region including several kilobases of nucleotide sequence upstream of an expressed gene will include the promoter responsible for driving expression of that gene. For example, Applicants have previously provided in support well known examples of 5′ flanking regions of plant genes that are about 1.2 kb or less, and were selected for promoter analysis by those skilled in the art. (see pp. 106, 291, and 503, in *Control of Plant Gene Expression* (1993), ed. Desh Pal Verma, CRC Press, previously submitted). Further, the Benfey and Kim references previously cited described regulatory elements within about one- to several hundred bases upstream of the transcription initiation site. Thus, Applicants have provided evidence that the sequence of SEQ ID NO:1 contains a promoter. In contrast, the Office Actions in this case have not provided any evidence to contradict the

teachings in the specification and in the art that this 2.8 kb region upstream of an expressed gene contains a promoter.

Applicants note that MPEP § 2164.04 provides that the Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. This is in accordance with *In re Marzocchi*, 169 USPQ 367 (CCPA 1971), where the court held that "it is incumbent on the Patent Office, whenever a rejection on this basis [enablement] is made to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertion of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." 169 USPQ at 370. In the present case, Applicants have provided evidence that one of skill in the art would accept as conclusive that SEQ ID NO:1 has promoter activity; particularly, that this sequence naturally occurs upstream from an expressed gene (see, *e.g.*, specification pp. 15-16 and the Examples from pp. 25-42). Thus, the assertion in the Office Action (page 5) that the "specification has provided no evidence of promoter activity for the disclosed nucleotide sequence" is unsubstantiated and incorrect. Because this assertion is unsubstantiated, a *prima facie* case of lack of enablement has not been established. Applicants invite the Examiner to submit an affidavit under 37 C.F.R. § 1.104(d)(2) in support of this statement if the rejection of claims 1-23 for lack of enablement under 35 U.S.C. § 112, first paragraph, is maintained on this ground.

The Office Action concludes (pp. 5-6) by stating that assessment of promoter activity

> [I]s far from routine experimentation, but would require undue trial and error experimentation to test the myriad of different sized fragments from different regions of the upstream region, and to screen through the vast number of transformed cells, tissues, or plants, to identify those upstream regions which possess promoter activity. Therefore, the invention is not enabled.

It seems from this discussion that the Office Action wishes that Applicants had identified and claimed a minimal promoter, *i.e.*, the minimum amount of upstream sequence necessary for promoter activity. However, Applicants' present claims are not drawn to a minimal promoter but are rather drawn to a promoter sequence comprising the sequence set forth in SEQ ID NO:1.

Applicants respectfully reiterate that the present claims meet the enablement requirement of 35 U.S.C. § 112, ¶1, and should be allowed.

Moreover, as stated in the previous Response, promoter activity may readily be determined by routine assays in which a putative promoter is linked to a reporter gene and expression of that reporter gene is measured. Contrary to the conclusion expressed in the Office Action, such an assessment is routine in the art and would not require "undue trial and error experimentation." As noted previously by Applicants, the routine nature of this assessment is illustrated by myriad articles in the art, including the Benfey and Kim references cited previously in this case.

The appropriate standard for determining whether undue experimentation would be required to make and use an invention has been discussed by the Federal Circuit in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and *In re Jackson*, 217 USPQ 804, 807 (Bd. Pat. App. & Int. 1982). In *In re Jackson*, the Board held that a considerable amount of experimentation is permitted to practice the invention and is not undue if it is merely routine in the art or if the specification provides a reasonable amount of guidance and direction to perform such experimentation. Applicants note that it is now customary in the art to make and assay a number of sequences for a desired function in order to achieve the best results. For example, such techniques can involve what is commonly referred to as "shuffling," as described for example in U.S. Patent No. 5,837,458, issued November 17, 1998 with inventors Minshull and Stemmer and entitled, "Methods and Compositions for Metabolic and Cellular Engineering." In such techniques, it is common to mutagenize individual sequences or a set of sequences which are then assayed for a desired activity. In fact, such techniques may even make use of a library of sequences which is recursively mutagenized, screened for function using a functional assay, and re-mutagenized. Examples of the use of such techniques include: Minshull and Stemmer (1999) *Current Opinion in Chemical Biology* 3:284-290, entitled "Protein Evolution by Molecular Breeding"; and Christians *et al.* (1999) *Nature Biotechnology* 17: 259-264, entitled "Directed evolution of thymidine kinase for AZT phosphorylation using DNA family shuffling." Such experiments are designed and are intended to encompass the generation and testing of a very large number of variant sequences for a desired function. As indicated by these and other

publications, this degree of experimentation is now considered routine in the art and thus would not be considered "undue experimentation" under *In re Wands* and *In re Jackson*.

In light of the discussion above, it is apparent that those of skill in the art would not consider the amount of experimentation to determine whether a given polynucleotide fell within these claims to be undue. Accordingly, the rejection of claims 1-23 should be withdrawn and should not be applied to the new claims.

In light of the above statements, Applicants respectfully assert that the present specification does meet the statutory enablement and written description requirements. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections of the claims under 35 U.S.C. §112.

The Rejection of Claims Under 35 U.S.C.§112, Second Paragraph, Should Be Withdrawn

The Office Action (9/24/03, page 6, #4) has rejected claim 24 as being indefinite for its recitation of "stringent conditions." Applicants note that claim 24 has been canceled. Accordingly, this rejection has been obviated by amendment.

Consideration Of Previously Submitted Information Disclosure Statement

It is noted that an initialed copy of the PTO Form 1449 that was submitted with Applicants' Information Disclosure Statement filed October 4, 1999 and again on January 16, 2001, has not been returned to Applicants' representative with the Office Action. Applicants note that the Office Action (9/24/03, page 2, #1) stated that the IDS and copies of references had not been received into the application. Applicants are providing herewith copies of the references along with the postcard receipt and original IDS filed 10/4/99. Accordingly, it is requested that an initialed copy of the Form 1449 be forwarded to the undersigned with the next communication from the PTO.

CONCLUSION

In view of the above amendments and remarks, Applicants submit that the rejections of the claims under 35 U.S.C. §§112, first and second paragraphs, are overcome. Applicants respectfully submit that this application is now in condition for allowance. Early notice to this effect is solicited.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject Application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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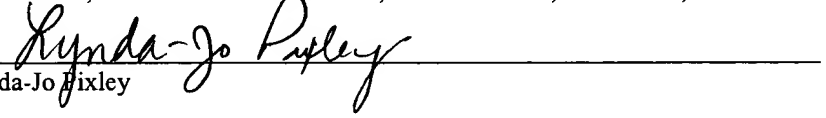

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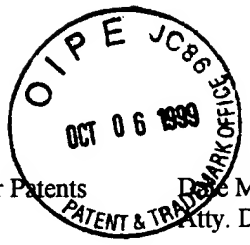

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Application No. 09/327,230; Filing Date 06/07/99
Inventor(s): Gray et al.; Title of Invention: METHODS AND COMPOSITIONS FOR CONTROLLING CELL DEATH AND DISEASE RESISTANCE IN PLANTS
Documents Enclosed: Declaration with cover - 5 pages / Form 1449 and IDS Cover - 3 pages / 1 page copy of Notice to File Missing Parts

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